

**THE ASSESSMENT OF A NOVEL *IN SITU* FORMING WOUND DRESSING FOR
MILITARY USE
FOR THE
26th ARMY SCIENCE CONFERENCE**

**Sameer Shums*, John Jackson, Arthur Lu, Xiaowen Zhai, Thomas Hirt and Fiona Carney
BioCure, Inc.
Norcross, GA. 30071**

1. ABSTRACT

Presented is an evaluation of the biocompatibility and physical properties of a novel hydrogel which cures *in situ* to form an effective wound dressing. This dressing has the capability of meeting the needs of both the far forward soldier and for use in hospital settings. The GelSpray™ product platform was developed by BioCure, Inc. [Norcross, GA.] in concert with the Center for Military Biomaterials Research (CeMBR).

The GelSpray™ formulation has been cleared by the US Food & Drug Administration and is indicated for minor cuts and scrapes and minor irritations of the skin. While additional characteristics, such as antimicrobial properties and drug release, and applications for complex wounds are presented in this document, these results are based upon preliminary evaluations and have not been reviewed by the FDA and warrant additional testing.

2. INTRODUCTION

The process for normal wound healing is highly structured and the phases proceed in a delicate balance to one another. The four phases of wound healing begin immediately upon wounding and are categorized as hemostasis, inflammation, proliferation, and remodeling. This process is well defined and exhaustively studied and at times may be easily interrupted by systemic pathologies capable of impairing normal wound healing. Wounds inflicted on military personnel represent a unique challenge to current wound healing methodologies and commercially available dressings. The far-forward soldier's ability to treat injuries are commonly plagued by wound location, delayed treatment, contamination by foreign objects, debris and bacteria and by complex, multifaceted wounds that pre-formed gauze and bandages are not capable of treating.

BioCure's GelSpray™ Wound Dressing offers a fast-curing, polymer-based dressing capable of addressing

various wound etiologies and is intended for self-application. As a platform product, the dressing is made of a biocompatible hydrogel based on polyvinyl alcohol. The hydrogel dressing provides the necessary mechanical requirements of a dressing capable of treating the soldier's wounds. Applied as a liquid from a syringe or a custom-designed military device, the dressing cures rapidly providing full contact with the wound margins and periwound site. Additionally, the hydrogel dressing provides and maintains a moist wound environment which is known to promote wound healing. The dressing is removed as one cohesive unit providing debridement of the wound bed.

Many advanced wound dressings to date utilize hydrogels because they are effective, comfortable, easy to use and cost effective solutions for complex wounds. These dressings provide control of wound surface hydration by both donating moisture as needed and absorbing excess wound exudate. Hydrogel dressings have been proven effective in facilitating the repair of pressure ulcers, diabetic ulcers, and burns, and they have supplanted saline-moistened gauze for many applications. BioCure has broken from the ranks of preformed hydrogel dressings, and has developed an *in situ* polymerizing dressing. This type of dressing is intended to provide full coverage of the wound and periwound site, provide wound packing capabilities for deep wounds, and adherence to intact skin rather than the wound bed to prevent re-injury during removal. Additionally the dressing is highly elastic and conformal when applied to highly jointed areas such as hands, wrists and elbows, where small movements typically cause preformed bandages to fail.

3. METHODS & MATERIALS

3a. BIOCOMPATIBILITY

Biocompatibility assessment of the GelSpray™ formulation was performed in accordance to the ISO

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10993 standard for Biological Evaluation of Medical Devices. The formulation was specifically evaluated for cytotoxicity [Part 5], sensitization [Part 10], irritation [Part 10] and muscle implant [Part 6].

3b. ANTIMICROBIAL ACTIVITY

An iteration of the GelSpray™ formulation containing silver salts was assessed utilizing in vitro assays. A Kirby-Bauer Zone of Inhibition study was performed against ATCC strains of *Pseudomonas Aeruginosa* [10145U] and *Staphylococcus Aureus* [29213]. In both instances, a lawn concentration between 10^7 to 10^8 CFU was grown in agar plates. Preformed Ampicillin disks were utilized as a positive control for *S. Aureus* and a 50% Clorox bleach solution served as the positive control for the *Ps. Aeruginosa* plates. Disks hydrated with USP water served as the negative controls for both strains.

The GelSpray™ dressing was also evaluated in a barrier study utilizing a non-GLP, pilot porcine model conducted at the University of Miami. The barrier study illustrates the dressing's ability to prevent bacteria from penetrating through the dressing into the wound bed. The partial thickness wounds were created using an electrokeratome [customized Storz Instruments dermatome] with a 0.7mm blade and n=9 wounds per test article. The test articles were the GelSpray™ and GelSpray™ with silver salts with the negative and positive control of 3M's transparent 1624W Tegaderm™ (untreated) and surgical sponge gauze respectively. The Tegaderm dressing was also used to cover the GelSpray test articles to prevent incidental removal from the swine. Wound dressings were applied, as per the manufacturer's instructions, and 100µl of a 1×10^8 CFU suspension of *Ps. Aeruginosa* (ATCC 27312) in saline which was applied to the external surface of the dressing. At 24 and 48 hour intervals a minimum of 4 dressings were removed and the wound bed was washed for presence of *Ps. Aeruginosa*. Serial dilutions of the wash extract were performed and the CFU/mL was counted.

3c. PHYSICAL PROPERTIES

To manage a moist wound environment, the GelSpray™ formulation was evaluated for Moisture Uptake (MU) and Moisture Vapor Transmission Rate (MVTR) and all results were compared to Johnson & Johnson's Tielle™ Hydropolymer Dressing. The Tielle™ dressing is a preformed polyurethane absorbent island with a breathable adhesive backing.

The moisture uptake protocol was based upon a modification to US Patent 20040142019 (Xylos Corp. (Watervliet, NY) Serafica, Ganzalo; *et al*). The MU studies were performed at room temperature and 90-95% relative humidity and measured as water gain over per unit area of the dressing (g/cm^2).

The Moisture Vapor Transmission Rate (MVTR) was performed per ASTM D1653 using an inverted container method. The MVTR test was performed at 23°C & 50% relative humidity for 24 hours with results expressed in water vapor loss over area for 24 hours ($\text{g}/\text{m}^2/24\text{hr}$).

As illustrated in the barrier study, the adhesion of the dressing is critical to ensure debris and bacteria do not migrate into the wound bed, while also ensuring the wound bed is not re-injured from excessive adhesive forces when the dressing is removed. Adhesion testing was performed based upon a modification to ASTM D-330/D3330M-04. This procedure calls for defatted pig skin to be used as a substrate for application of the dressing and describes the procedure for conditioning the skin and dressing prior to testing. The GelSpray™ dressing was tested after 1 and 4 hours as the adhesive forces increase as the hydrogel dressing loses its moisture content around the wound bed, unlike adhesive-based dressings, which retain the same adhesion over time.

3d. DRUG RELEASE

An iteration of the GelSpray™ formulation was used to deliver a small chain peptide (Mw ~1400) designated Homspera®, [ImmuneRegen® BioSciences, Inc.] intended to promote wound healing. Bioactivity tests were carried out in order to make sure that the peptide was successfully released from the dressing without fouling or degradation.

An in vitro assessment for the release of lidocaine from the GelSpray™ formulation for pain management was also evaluated. The properties of the GelSpray™ dressing can be tailored to release the small molecular weight drug in a controlled manner.

4. RESULTS & DISCUSSIONS

4a. BIOCOMPATIBILITY

The GelSpray™ formulation passed all required biocompatibility studies, specifically for cytotoxicity,

sensitization, irritation and muscle implant. All studies were performed under Good Laboratory Practices.

4b. ANTIMICROBIAL ACTIVITY

The GelSpray™ with silver salts was successful in demonstrating both contact kills when a drop was placed on the bacteria, as well as a diffused kill when the formulation was placed in an agar well.

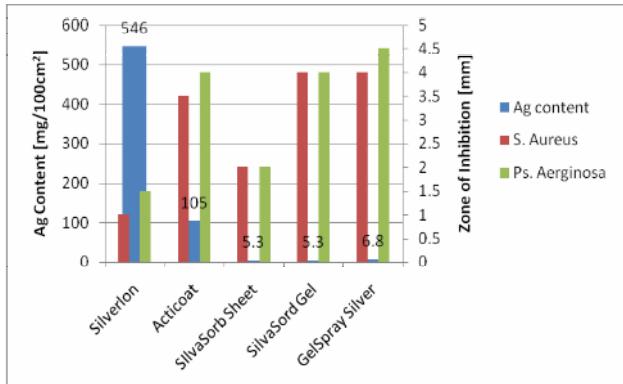


Figure 1: Silver content for the GelSpray™ with silver salts and commercially available dressings and the respective zone of inhibition.

GelSpray™ product showed a 2.5 log reduction in *Ps. Aeruginosa* within the barrier studies, while the antimicrobial GelSpray™ with silver salts showed a 6.5 log reduction as compared to the gauze control.

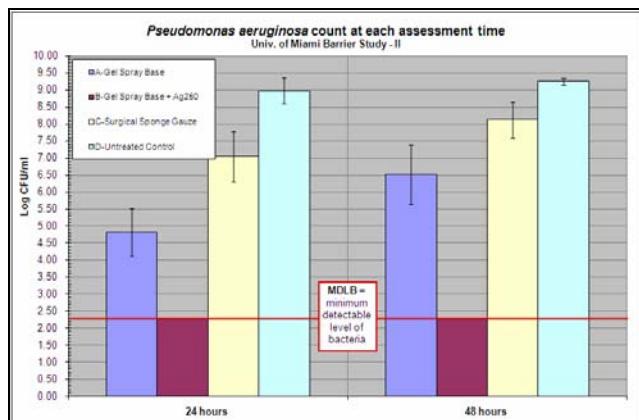


Figure 2: Barrier results at 24 & 48 hours against *Ps. Aeruginosa* assessment for GelSpray™ Base (dark blue), GelSpray™ with silver salts (maroon), surgical sponge gauze (yellow) and an untreated area (light blue).

4b. PHYSICAL PROPERTIES

The Moisture Uptake for the GelSpray™ dressing was significantly ($p<0.05$) higher as compared to

the Tielle™ Hydropolymer dressing with an uptake of $0.16 \pm 0.01 \text{ g/cm}^2$ and $0.06 \pm 0.01 \text{ g/cm}^2$ respectively.

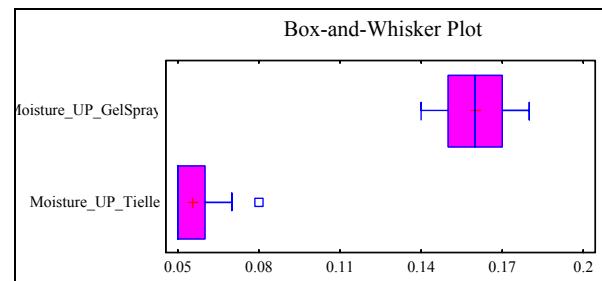


Figure 3: Box-and-Whisker plot comparing the GelSpray™ base dressing to the Tielle™ Hydropolymer dressing for moisture uptake properties.

The MVTR of the GelSpray™ dressing was significantly ($p<0.05$) greater than that of the Tielle™ dressing with 245 ± 35 and $75 \pm 9 \text{ g/m}^2/24\text{hr}$ respectively.

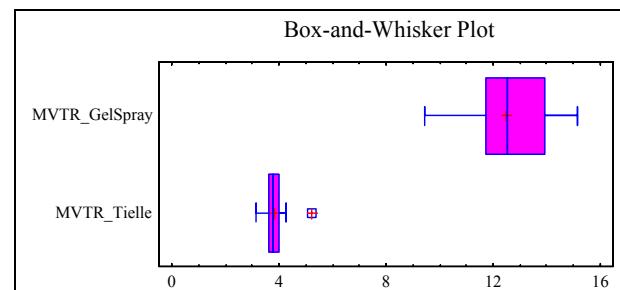


Figure 4: Box-and-Whisker plot comparing the GelSpray™ base dressing to the Tielle™ Hydropolymer dressing for the moisture vapor transmission rate.

The adhesive force of the GelSpray™ dressing was significantly ($p<0.05$) greater than that of the Tielle™ dressing with $0.33 \pm 0.12\text{N}$ at 1 hour after application and $3.66 \pm 1.59\text{N}$ at 4 hours after application versus $0.23 \pm 0.07\text{N}$ for the Tielle™ Hydropolymer dressing.

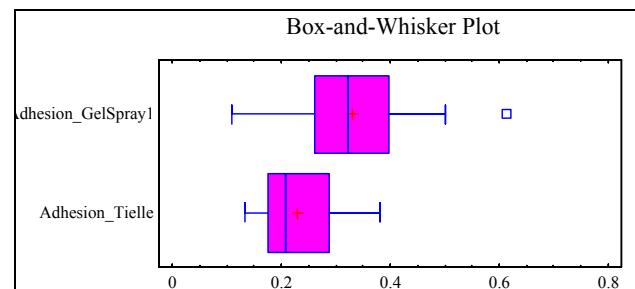


Figure 5: Box-and-Whisker plot comparing the GelSpray™ base dressing to the Tielle™ Hydropolymer dressing for adhesive force at 1 hour.

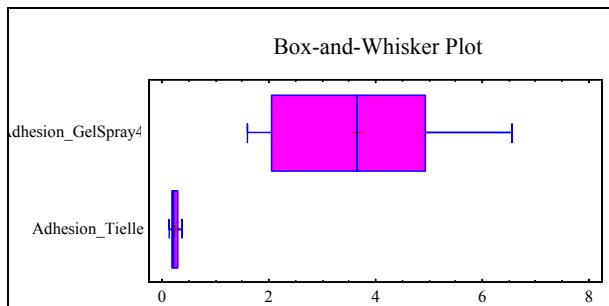


Figure 6: Box-and-Whisker plot comparing the GelSpray™ base dressing to the Tielle™ Hydropolymer dressing for adhesive force at 4 hours.

4c. DRUG RELEASE

The GelSpray™ dressing successfully released the wound healing peptide as illustrated by the HPLC analysis below. Bioactivity of the peptide was assessed to ensure there was no fouling or degradation of peptide in the dressing. The dressing quickly released about 50% of the small peptide drug after 1 hour. The release gradually slowed over time and ultimately provided a 70% within the first 20 hours (Figure 7). The properties of the GelSpray™ dressing can be tailored to control release of small peptide drug.

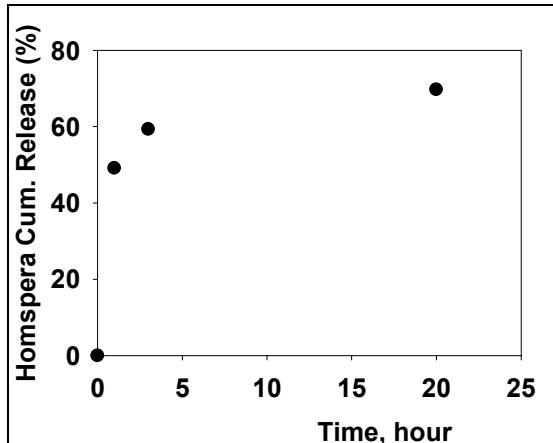


Figure 7: HPLC Plot illustrating the fast release of the small chain peptide from a modified GelSpray™ formulation.

An iteration of the GelSpray™ dressing was evaluated for releasing a small drug. Lidocaine was encapsulated into the dressing by forming a complex with a negatively charged polymer. Lidocaine can only be released from the PVA(-) gel in salt solutions by ion-exchange. Very little is released in pure water. This release is mainly controlled by the salt concentration and salt/lidocaine

ratio, making the GelSpray™ dressing release the small molecular weight drug in a controlled manner.

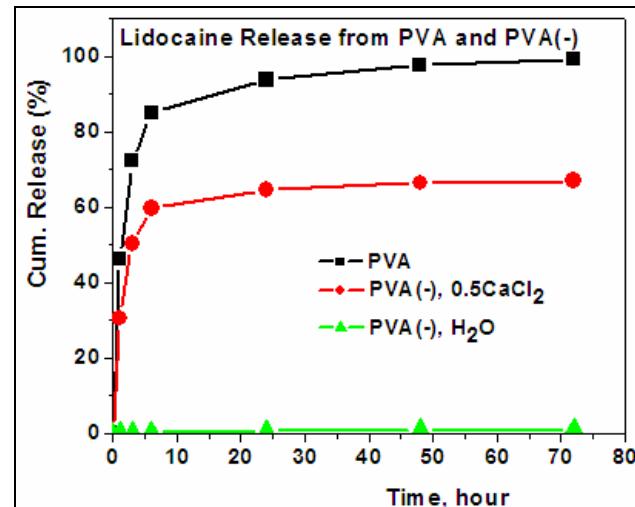


Figure 8: Release of lidocaine from PVA and PVA modified with negative charges.

GelSpray™ dressing offers a novel solution for the treatment of complex wounds such as those sustained in the battlefield environment. The dressing can be dispensed from an ergonomic two-part syringe or via a robust delivery device designed for the far forward soldier.



Figure 9: Two-part syringe delivery device for hospital use.

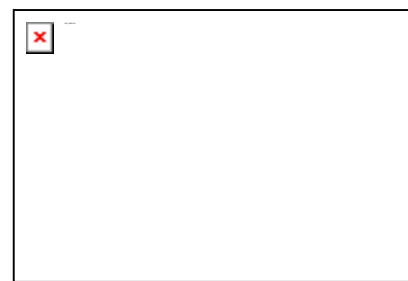


Figure 10: Conceptual delivery device for the far-forward soldier.

5. CONCLUSIONS

This data illustrates the GelSpray™ dressing's ability to create a moist wound environment and remain flexible without compromising its inherent adhesion properties to the periwound site. The dressing can also be removed in a cohesive manner providing effective debridement of the wound bed. The hydrogel formulation is an ideal carrier for various biologically active ingredients without compromising the mechanical or biocompatibility properties.

The GelSpray™ dressing shows superior MVTR and Moisture Uptake properties as compared to competitors, which are two critical characteristics in maintaining a moist wound environment to promote healing. The adhesion of the dressing ensures the dressing does not migrate nor will it allow debris or bacteria to enter the wound bed. Both GelSpray™ and the antimicrobial GelSpray™ with silver are excellent barriers to environmental infections.

Overall, BioCure's GelSpray™ dressing is a novel hydrogel-based wound dressing capable of addressing complex battlefield injuries and can be deployed by the far-forward soldier or hospital staff. The dressing's unique *in situ* application provides a competitive advantage over commercially available pre-formed dressings. Additionally, the base dressing allows for rapid use in the field and serves as a platform for the addition of active ingredients to address wound healing, pain, infection or bleeding.

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